REMARKS

I. Preliminary remarks

Claims 1-13 are pending in this application. Claim1 has been amended to recite "mammal" and "human." Support for these amendments may be found throughout the specification as filed and at, for example, page 32, lines 16-18; page 13, line 25; page 44, line 28; and page 55, line 2, of the published PCT.

No new matter has been introduced in this amendment.

II. The rejection of claims 1-13 under 35 USC 112, may be withdrawn.

Beginning at page 2 of the Office Action, the Examiner rejected claims 1-13 under 35 USC 112 as failing to comply with the enablement requirement. Specifically, the Examiner asserted that the claims do not require treatment and that it was unpredictable (citing Greco (J. Cellular Physiology, 2001, Vol. 187, pg 22-36), at the time the application was filed, as to how to obtain a therapeutic effect using GDEPT. The Examiner further asserted that the specification does not teach how much ADH expression, ethanol or acetaldehyde are required to treat a pre-existing tumor or how to administer a nucleic acid in the absence of cells to obtain toxicity. Applicants respectfully traverse.

Citing page 22, column 1, of Greco, the Examiner asserted that "Greco taught problems with gene therapy included delivery of a gene to the tumor...". However, Greco at pg. 22, col. 1 simply states "for gene therapy three separate issues need to be considered..." Moreover, the first full paragraph of Greco, page 23, right-hand column, states: "For significant therapeutic gain, the released drug should be at least a 100-fold more toxic than the prodrug. The toxic agent should also have a half-life that allows diffusion to the surrounding untransfected cells (bystander effect), but ensure that any drug escaping into the circulation will be inactive. Moreover, the induced cytotoxocity should be cell cycle phase- or proliferation-independent, to kill a wide range of tumor cell populations" [emphasis added]

The present invention meets all of these requirements. It is clear from Greco that with these parameters significant therapeutic gain is achievable. Therefore Greco does

not cast doubt on the enablement of the present invention. Applicants also point out that the present invention does not relate to a method of delivering a gene to a tumor. Rather, the invention of the present application relates to the use of acetaldehyde in a mammal as a toxin, whereby a nucleic acid encoding an enzymatically active portion of human alcohol dehydrogenase and ethanol are administered to the mammal. This had never been taught before, and for the application to be limited to a specific mode of delivery of a gene to a tumor cell would be unduly limiting.

In further support of the assertion that the methods of the present invention are non-enabled, the Examiner cited the instant application at page 63, lines 16-21: "the specification teaches accurate assessment of cytotoxic effects of exposure to acetaldehyde is extremely difficult in vitro because acetaldehyde is volatile...". However, in fact this section on page 63, lines 16-21 recites "...the accurate assessment of the cytotoxic effects of prolonged exposure to acetaldehyde is extremely difficult **to quantify** in vitro." [emphasis added]. This passage does not mean that cytotoxic effects were not seen – just that the quantification was difficult to accurately assess. The specification continues to state (at page 63, lines 29-31) that "to obtain more clinically meaningful data we examined a simple pre-clinical method..."

Finally, Applicant's submit that although dosing of drugs is part of a clinician's routine duties, ethanol dosages are discussed at least on page 64, lines 10-11, and likely ADH levels are discussed on page 64, lines 20-21.

In view of the above arguments, Applicant's respectfully submit that the rejection of claims 1-13 under 35 USC 112, may be withdrawn.

III. The rejection of claims 1 and 8 under 35 USC 102(b), may be withdrawn.

Beginning at page 4 of the Office Action, the Examiner rejected claims 1 and 8 under 35 USC 102(b) as being anticipated by Mapoles. Specifically, the Examiner asserted that Mapoles introduced a plasmid containing ADH into a culture of cells and damaged cells expressing ADH when exposed to alcohol, and that acetaldehyde exposure inhibited growth of the cells. Applicants respectfully traverse.

The Examiner, at page 5 of the Office Action, interpreted the term "subject" in the claims to include the "cell culture" in Mapoles. Although the Applicants do not agree with this assertion, claim 1 has been amended to replace the term "subject" with "mammal". In addition, claim 1 has been amended to recite the term "human" prior to alcohol dehydrogenase (ADH). Mapoles uses mouse ADH (see page 633, LHC, 2nd full paragraph).

In view of the above arguments and amendments, Applicant's respectfully submit that the rejection of claims 1 and 8 under 35 USC 102(b), may be withdrawn.

IV. The rejection of claims 1 and 4-9 under 35 USC 103(a), may be withdrawn.

Beginning at page 5 of the Office Action, the Examiner rejected claims 1 and 4-9 under 35 USC 103(a) as being unpatentable over Philipott in view of Greco and Yokoyama. Specifically, the Examiner asserted that Philipott administered ADH via ADEPT to tumor cells. As discussed previously, the Examiner also asserted that Greco described GDEPT. The Examiner further asserted that the nucleotide sequence of ADH was disclosed in Yokoyama. Applicants respectfully, traverse.

Applicant's first point out that Philipott administered an ADH antibody (protein) – not a nucleic acid as taught in the present invention. Further, Philipott uses horse ADH (see page 39, RHC line 5 of the 2nd paragraph in the section entitled "Materials and Methods"), while the presently amended claims recite "human" ADH. Importantly, Philipott's method teaches the conversion of allyl alcohol to acrolein. Philipott's method, therefore, does not teach or suggest the conversion of ethanol to acetaldehyde as per the present invention using human ADH. Allyl alcohol is not ethanol; one cannot use allyl alcohol as a substance according to the present invention because once ingested/administered, the ADH in a mammal's liver would transform the allyl alcohol to acrolein and would likely kill the mammal.

As discussed above, none of the cited references teach the use of acetaldehyde in a mammal as a toxin whereby a nucleic acid encoding an enzymatically active portion of human alcohol dehydrogenase and ethanol are administered to the mammal. In particular,

none of the cited references teach that the substrate should be ethanol and that the toxin should be acetaldehyde.

In view of the above arguments and amendments, Applicant's respectfully submit that the rejection of claims 1 and 4-9 under 35 USC 103(a), may be withdrawn.

CONCLUSION

In view of the above amendment, applicant believes the pending application is in condition for allowance.

Dated: December 29, 2008

Respectfully submitted,

By _____
Eric M. Brusca
Registration No.: 52,664
MARSHALL, GERSTEIN & BORUN LLP
233 S. Wacker Drive, Suite 6300
Sears Tower
Chicago, Illinois 60606-6357
(312) 474-6300
Attorney for Applicant